Complete Summary

GUIDELINE TITLE

Managing asthma during pregnancy: recommendations for pharmacologic treatment.

BIBLIOGRAPHIC SOURCE(S)

National Asthma Education and Prevention Program. Managing asthma during pregnancy: recommendations for pharmacologic treatment. Bethesda (MD): National Heart, Lung, and Blood Institute; 2005 Jan. 57 p. [129 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On November 18, 2005, the U.S. Food and Drug Administration (FDA) notified manufacturers of Advair Diskus, Foradil Aerolizer, and Serevent Diskus to update their existing product labels with new warnings and a Medication Guide for patients to alert health care professionals and patients that these medicines may increase the chance of severe asthma episodes, and death when those episodes occur. All of these products contain long-acting beta2-adrenergic agonists (LABA). Even though LABAs decrease the frequency of asthma episodes, these medicines may make asthma episodes more severe when they occur. A Medication Guide with information about these risks will be given to patients when a prescription for a LABA is filled or refilled. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Asthma during pregnancy and lactation

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Anesthesiology
Emergency Medicine
Family Practice
Internal Medicine
Obstetrics and Gynecology
Pediatrics
Preventive Medicine
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

To improve asthma care and the quality of life for pregnant and lactating women with asthma and their families

TARGET POPULATION

Pregnant or lactating women with asthma

INTERVENTIONS AND PRACTICES CONSIDERED

General Management

1. Use of stepwise approach to therapy

2. Patient education
3. Referral to an asthma specialist
4. Appropriate use of metered dose inhaler or nebulizer
5. Identification and control of factors contributing to asthma severity
6. Hospital/emergency room admission criteria
7. Appropriate patient follow-up

Assessment and Monitoring

1. Assessment of signs and symptoms
2. Measurement of forced expiratory volume in 1 second (FEV_1)
3. Measurement of peak expiratory flow (PEF)
4. Pulse oximetry
5. Arterial blood gas analysis

Fetal Assessment

1. Electronic fetal monitoring
2. Biophysical profile
3. Ultrasound examinations
4. Assessment of fetal activity

Pharmacological Therapy

1. Short acting inhaled $beta_2$-agonists (albuterol, Bitolterol, levalbuterol (R-albuterol), pirbuterol)
2. Long acting inhaled $beta_2$-agonists (salmeterol, formoterol)
3. Systemic (injected) $beta_2$-agonists (epinephrine, terbutaline)
4. Anticholinergics (ipratropium bromide, ipratropium with albuterol)
5. Methylxanthines (theophylline)
6. Inhaled corticosteroids (budesonide dipropionate, beclomethasone, flunisolide, triamcinolone acetonide, fluticasone)
7. Oral (systemic) corticosteroids (methylprednisolone, prednisolone, prednisone)
8. Intravenous (IV) corticosteroids (hydrocortisone)
9. Cromolyn
10. Leukotriene receptor antagonists (montelukast, zafirlukast)
11. Second generation antihistamines (loratadine, cetirizine)
12. Nasal decongestants (oxymetazoline)

Other Interventions/Therapies

1. Inhaled oxygen
2. Intubation and mechanical ventilation

Interventions considered but not recommended:

- Chest x-ray
- Oral decongestants (Fexofenadine, Desloratadine, Azelastine)

MAJOR OUTCOMES CONSIDERED

Maternal health and fetal outcomes, including:

- Asthma symptom control
- Incidence of exacerbations
- Asthma morbidity measures (hospital admissions, emergency room visits, physical activity level, lost work/school days)
- Pulmonary function
- Decrease in use of short acting $beta_2$-agonists
- Adverse effects of medications (including adverse effects on fetus)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature search, designed to be as comprehensive as possible, included both animal and human studies that were published in English in peer-reviewed medical journals. The search was performed by using key text words and Medical Subject Heading (MeSH) terms to identify all relevant studies. Key words included all anti-inflammatory and bronchodilator asthma medications (systemic beta-agonists were not included because they are not recommended therapies for managing asthma in adults), teratology, fetus, fetal outcomes, congenital abnormalities, lactation, breast milk, breast feeding, and pregnancy outcomes. Publications in 1990 through May 2003 were searched in five databases: PubMed, TOXLINE (core and special), and Developmental And Reproductive Toxicology (DART; core and special).

The search retrieved titles of 6,223 references. Of these, 100 references were identified as journal review articles and moved to a separate bibliography. References identified as letters, meeting abstracts, or book chapters were excluded. Titles of the remaining references were then screened for relevance to the topic of safety of asthma medication during pregnancy. Each title was considered by two reviewers; if both agreed the reference was relevant, it was flagged for subsequent abstract review. A difference of opinion between the reviewers also resulted in retaining a reference for abstract review.

On the basis of the review of titles, 226 references were flagged, and abstracts for all were retrieved. Each abstract was rated independently by two Working Group members on the basis of relevance to the search question and whether the data appeared to support a change to current guidelines recommendations. A difference of opinion between two reviewers on the merits of an abstract was generally resolved by a larger group discussion. A few abstracts were rated as inconclusive, however, because information was insufficient without reviewing the full article. Abstracts rated as either relevant or inconclusive were flagged for subsequent review of the full article.

After the review of abstracts, 55 references were flagged for review of the full article. At this point, a quality control measure also was implemented. To ensure further that no relevant studies were overlooked, this measure involved going back to the bibliography of 100 review articles and retrieving those articles with publication dates of 1998 or later. Twenty-two articles were retrieved; they were reviewed by Working Group members for the purpose of identifying possible citations missed during the basic review process. This step identified 25 potential new references; of these, 9 were deemed relevant and therefore were added to the full-article review.

Sixty-four references underwent a full article review by a primary and a secondary reviewer. Of these 64 references, 42 met the study selection criteria for inclusion in the systematic review of the evidence.

Subsequent to May 2003 and prior to a final draft of the report in March 2004, two additional articles that met the study selection criteria were published and included in the systematic review of the evidence. Thus, the total number of articles abstracted to evidence tables was 44.

NUMBER OF SOURCE DOCUMENTS

44

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Evidence Category A: Randomized controlled trials, rich body of data. Evidence is from the endpoint of well-designed randomized controlled trials that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.

Evidence Category B: Randomized controlled trials, limited body of data. Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of randomized controlled trials, or meta-analysis of randomized controlled trials. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendations, or the results are somewhat inconsistent.

Evidence Category C: Nonrandomized trials and observational studies. Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.

Evidence Category D: Panel consensus judgment. This category is used only where the provision of some guidance was deemed valuable, but the clinical literature addressing the subject was insufficient to justify placement in one of the

other categories. The consensus is based on clinical experience or knowledge that does not meet the criteria for categories A through C.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data from the articles were abstracted to evidence tables by an outside contractor and were recorded in an electronic database. All of the evidence tables are available for online retrieval at http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg.htm.

Data elements included categories such as study design and methods, patient characteristics, lung function outcomes, symptom outcomes, medication outcomes, utilization outcomes, and adverse events.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In August 2003, the Working Group met in Bethesda, MD, to discuss the systematic review of the evidence from safety studies and to interpret the implications for updating the recommendations of the Asthma and Pregnancy Report 1993 and adapting the recommendations for a stepwise approach to managing asthma presented in the Expert Panel Report (EPR) -- Update 2002. The Working Group agreed to note the level of the evidence used to justify Working Group recommendations in parentheses following the initial recommendation for a specific medication.

Development of these recommendations was an iterative process of drafting, reviewing, and building consensus. In the summer and fall of 2003, the Working Group writing committees drafted their respective sections of the report through electronic mail and telephone conference calls. The Working Group reviewed and revised drafts through telephone conference calls and subsequent electronic mails among the full Working Group membership. During the calls, votes were taken to ensure agreement with final recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

In November 2003, a draft report was mailed to the National Asthma Education and Prevention Program (NAEPP) Science Base Committee and three consultants with a specialty in maternal and fetal medicine. The Science Base Committee met by conference call to review the draft report, and the consultants mailed their comments. All comments were discussed by the Working Group in a December 2003 conference call, and agreement was reached on how to address the comments.

In January 2004, a revised draft report was sent to the Science Base Committee for their final review, and in February 2004 the report was mailed to the NAEPP Coordinating Committee for its review and endorsement. In a March 2004 conference call, the Working Group reviewed and addressed all NAEPP Coordinating Committee comments, and the report was completed.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the levels of evidence (A-D) supporting some of the recommendations are provided at the end of the "Major Recommendations" field.

Managing Asthma During Pregnancy

General Principles

- The treatment goal for the pregnant asthma patient is to provide optimal therapy to maintain control of asthma for maternal health and quality of life as well as for normal fetal maturation throughout gestation. Asthma control is defined as:
    - Minimal or no chronic symptoms day or night
    - Minimal or no exacerbations
    - No limitations on activities; no school or work missed
    - Maintenance of (near) normal pulmonary function
    - Minimal use of short-acting inhaled beta$_2$-agonist
    - Minimal or no adverse effects from medications
- Recommendations for pharmacologic therapy are intended to be general guidelines to assist clinical decision making. They are not intended to be prescriptions for treatment or to replace individualized treatment plans. Asthma is highly variable. Specific therapy should be tailored to the needs and circumstances of individual patients. A general stepwise approach to therapy is recommended in which the number and dose of medications used are increased as necessary and decreased when possible, based on the severity of the patient's asthma. (See appendix B in the original guideline document, figures 1, 2, and 3 for long-term asthma management and figures 4, 5, and 6 for management of acute exacerbations.)

- Pharmacologic therapy should be accompanied at every step of severity by patient education and measures to control those factors that contribute to the severity of the asthma.
- Asthma care should be integrated with obstetrics care, in the opinion of the Working Group. The obstetrical care provider should be involved in asthma care and should obtain information on asthma status during prenatal visits. Information should include day and nighttime symptoms, peak flow measures or spirometry reading, and medication usage. Consultation or co-management with an asthma specialist is appropriate, as indicated, for evaluation of the role of allergy and irritants, complete pulmonary function studies, or evaluation of the medication plan if there are complications in achieving the goals of therapy or the patient has severe asthma. A team approach is helpful if more than one clinician is managing the asthma and the pregnancy.

Four Components of Asthma Management

Objective Measures for Assessment and Monitoring

In the opinion of the Working Group, patients who have persistent asthma should be evaluated at least monthly during pregnancy. A major reason for this frequency of monitoring is that the course of asthma changes in approximately two-thirds of women during pregnancy. Evaluation should include a history (symptom frequency, nocturnal asthma, interference with activities, exacerbations, and medication use), lung auscultation, and pulmonary function. The dyspnea in pregnancy may seem similar to the dyspnea experienced during asthma exacerbations, but the dyspnea of pregnancy is not associated with the chest tightness, wheezing, and airway obstruction characteristic of asthma. Spirometry tests are recommended at the time of the initial assessment. For routine monitoring at most subsequent follow-up outpatient visits, spirometry is preferable, but measurement of peak expiratory flow (PEF) with a peak flow meter is generally sufficient. Patients with forced expiratory volume in one second (FEV_1) of 60-80 percent predicted are at increased risk of subsequent asthma morbidity during pregnancy, and patients with FEV_1 of less than 60 percent predicted are at even greater risk. Daily peak flow monitoring should be considered for patients with moderate to severe asthma, and especially for patients who have difficulty perceiving signs of worsening asthma. The evidence is not sufficient to conclude that peak flow monitoring is any more effective than symptom monitoring, but adequate studies in patients with moderate-to-severe asthma have not been conducted. For these patients, peak flow monitoring may be a valuable tool for home monitoring of asthma and communicating asthma status to the clinician. Because FEV_1 and PEF do not change appreciably due to pregnancy, PEF may still be a useful monitoring tool for pregnant women with asthma.

Women who have persistent asthma during pregnancy also may benefit from additional fetal surveillance in the form of ultrasound examinations and antenatal fetal testing. Because asthma has been associated with intrauterine growth rate (IUGR) and preterm birth, it is useful to establish pregnancy dating accurately by first trimester ultrasound where possible. In the opinion of the Working Group, the evaluation of fetal activity and growth by serial ultrasound examinations may be considered for (1) women who have suboptimally controlled asthma, (2) women with moderate to severe asthma (starting at 32 weeks), and (3) women after

recovery from a severe asthma exacerbation. The intensity of antenatal surveillance of fetal well-being should be considered on the basis of the severity of the asthma as well as any other high-risk features of the pregnancy that may be present. All patients should be instructed to be attentive to fetal activity.

Avoidance of Factors Contributing to Asthma Severity

Identifying and avoiding factors that can contribute to asthma severity ("asthma triggers") can lead to improved maternal well-being with less need for medications. (Refer to appendix B in the original guideline document, figure 7, Summary of Control Measures for Environmental Factors That Can Make Asthma Worse.) In previously untested patients, either prick skin tests or in vitro (radioallergosorbent test [RAST] or enzyme-linked immunosorbent assay [ELISA]) tests may be performed to identify relevant allergens (e.g., mites, animal dander, mold, cockroaches) for which specific environmental control instructions can be given. If the patient is using allergen immunotherapy for the control of allergies, it can be continued during pregnancy. However, benefit-risk considerations do not generally favor beginning immunotherapy during pregnancy because the initiation of immunotherapy can be associated with anaphylaxis, which can be fatal to the mother and fetus.

Smokers must be encouraged to discontinue smoking, and all patients should try to avoid, as much as possible, exposure to environmental tobacco smoke and other potential irritants. Morbidity during pregnancy due to smoking may be independent of and additive to morbidity due to asthma. Furthermore, maternal smoking may be associated with increased risk for wheezing and development of asthma in her child.

Patient Education

It is recommended that the clinical team members help to ensure that the pregnant woman has access to education about asthma so that she can understand the potential interrelationships between asthma and pregnancy. Controlling asthma during pregnancy is important for the well-being of the fetus. The woman should understand that it is safer to be treated with asthma medications than it is to have asthma symptoms and exacerbations. To prevent maternal and fetal hypoxia, she should be able to recognize and promptly treat signs of worsening asthma. She should have a basic understanding of medical management during pregnancy, including self monitoring and the correct use of inhalers. The pregnant patient should be given an individualized action plan that is based on a joint agreement between the patient and the clinician about the goals of therapy and treatment. The patient should have prompt access to her clinician for uncontrolled symptoms. The patient should also understand how she can reduce her exposure to or control those factors ("asthma triggers") that contribute to her asthma's severity.

Pharmacologic Therapy

It is safer for pregnant women with asthma to be treated with asthma medications than to have asthma symptoms or exacerbations and reduced lung function that may potentially impair oxygenation for the fetus. The type and amount of medication necessary to meet the goals of therapy are dictated by the

severity of the patient's asthma. (See appendix B in the original guideline document, figure 1 for classification of asthma severity and recommended treatment at each step.) Medications are categorized in two general classes: (1) long-term-control medications to achieve and maintain control of persistent asthma; especially important is daily medication to suppress the inflammation that is considered an early and persistent component in the pathogenesis of asthma; and (2) quick-relief medications that are taken as needed to treat symptoms and exacerbations. See the following section for recommendations about pharmacologic therapy during pregnancy at each step of asthma severity.

The Stepwise Approach to Gaining and Maintaining Control of Asthma

The stepwise approach to therapy, in which the dose and number of medications and frequency of administration are increased as necessary and decreased when possible, is used to achieve and maintain asthma control. The effectiveness of medications is assumed to be the same in pregnant women as in nonpregnant women, although there are no studies that directly test this assumption. Refer to Appendix B, figures 1, 2, and 3 of the original guideline document for a summary of the recommended therapies and medication dosages in the stepwise approach to long-term management of asthma during pregnancy and lactation.

Gaining Control of Asthma

The pregnant patient with asthma poses unique challenges for the clinician. The clinician judges individual patient needs and circumstances to determine at what treatment step to initiate therapy, while focusing on the health and well-being of both the mother and the fetus. Assessment of the patient's asthma history, current symptoms, and objective measures are all important in making this determination. For example, pregnant women with asthma may have minimal symptoms but still have abnormal pulmonary function tests and potentially impaired oxygenation.

Continual monitoring is useful to ensure that asthma control is achieved. Asthma control is best indicated by patient history (i.e., symptom frequency, amount of medication used) and by repeated pulmonary function measures (PEF or spirometry). If control is not achieved with initial therapy (e.g., within 1 month) or sufficient symptom reduction within 5-7 days of initiating or changing the therapeutic plan, then the plan, patient adherence, and possibly the diagnosis should be reevaluated.

Maintaining Control of Asthma

Maintain the Treatment

Once control is achieved and sustained for several months, a step down to less intensive therapy is encouraged for nonpregnant patients to identify the minimum therapy for maintaining control. A similar step-down approach should be considered for pregnant patients; however, such a step down should be undertaken cautiously and gradually to avoid compromising the stability of the patient's asthma control. For some patients, it may be prudent to postpone, until after the infant's birth, attempts at reducing therapy that is effectively controlling the patient's asthma.

Regular Follow-up Visits (at 1- to 2-Month Intervals) Are Important

Clinicians need to assess whether control of asthma has been maintained and whether an alteration in the patient's therapy is appropriate. Clinicians also need to monitor and review the action plan for daily self management and response to worsening signs of asthma, the medications, and the patient's self-management behaviors (e.g., inhaler and peak flow monitoring techniques as well as actions for controlling factors that aggravate one's asthma). More frequent clinician-patient visits will depend on the patient's response to the prescribed treatment regimen(s) and the time of gestation. Depending on the severity of the underlying maternal asthma, it is reasonable to expect that the patient's asthma may require closer monitoring and possibly more frequent medication dose adjustment as the pregnancy progresses. Furthermore, the varying stages of gestation may introduce additional physiologic changes in the patient that may indicate the need to adjust her medications.

If optimal control of asthma is not achieved and sustained at any step of care (as indicated by nocturnal symptoms, urgent care visits, or an increased need for short-acting $beta_2$-agonists), several actions may be considered.

- Review the plans for long-term asthma management and for responding to signs of worsening asthma to ensure that the clinician and patient are in agreement with the recommended actions. Assess patient adherence, and address those issues that may be affecting it.
- Assess the patient's technique in using medications correctly.
- Increase anti-inflammatory therapy temporarily if needed to reestablish control. A deterioration of asthma control may be characterized by gradual reduction in PEF or FEV_1, failure of inhaled $beta_2$-agonist therapy to produce a sustained response, reduced tolerance to activities, or increasing nocturnal symptoms. To regain control of asthma, a short course of oral prednisone may be warranted.
- Other factors that diminish control may need to be identified and addressed. Reassessment of specific asthma triggers or the identification of previously uninvolved triggers should be undertaken. Evaluate possible allergens, environmental pollution or smoking, patient or family barriers to adequate self-management behaviors, psychosocial problems, or newly prescribed or over-the-counter or herbal medications that might influence patient response.
- A step up to the next higher step of care may be necessary.
- Consultation with an asthma specialist may be indicated.

Intermittent Asthma

Step 1: Mild Intermittent Asthma

- A short-acting inhaled $beta_2$-agonist is used as needed to treat symptoms and is usually sufficient therapy for mild intermittent asthma (Level C evidence from safety studies in pregnancy).

  If effective in relieving symptoms and normalizing pulmonary function, intermittent use of short-acting inhaled $beta_2$-agonist can be continued on an as-needed basis. If significant symptoms recur or short-acting inhaled $beta_2$-

agonist is required for quick-relief treatment more than two times a week (with the exception of using inhaled $beta_2$-agonist to prevent exercise-induced bronchospasm), the patient should be moved to Step 2 of care.

- Albuterol is the preferred short-acting, short-duration $beta_2$-agonist for use during pregnancy (Level C evidence from safety studies in pregnancy).

  This drug is very selective for the $beta_2$-receptor and possesses an excellent safety profile for both pregnant and nonpregnant women with asthma. Although evaluations of drugs during pregnancy are limited, the greatest amount of efficacy and safety data during pregnancy exists with albuterol.

- Patients with intermittent asthma who experience exercise-induced bronchospasm benefit from using a short-acting inhaled $beta_2$-agonist shortly before exercise. During pregnancy, albuterol is also the preferred agent for treating exercise-induced bronchospasm.

Persistent Asthma

The Working Group recommends that patients with persistent asthma, whether mild, moderate, or severe, receive daily long-term-control medication. The most effective long-term-control medications are the inhaled corticosteroids, which diminish chronic airway inflammation and airway hyper-responsiveness. Strong evidence from clinical effectiveness trials supports the use of inhaled corticosteroids in nonpregnant adults with asthma. Reassuring efficacy and safety data from prospective cohort studies support using inhaled corticosteroids in pregnant women with asthma (Level C evidence from safety studies in pregnancy).

Quick-relief medication should be available to all patients with persistent asthma. Short acting inhaled $beta_2$-agonist (albuterol is preferred for pregnant women) is used as needed to relieve symptoms (Level C evidence from safety studies in pregnancy).

The intensity of treatment will depend on the severity of the exacerbation. (See section below on Managing Acute Exacerbations of Asthma During Pregnancy.) Use of short-acting inhaled $beta_2$-agonist on a daily basis, or increasing use, indicates the need for additional long-term-control therapy.

Step 2: Mild Persistent Asthma

- The preferred treatment for long-term control medication in Step 2 is daily low dose inhaled corticosteroid (Levels B and C evidence from safety studies in pregnancy).

  Proper technique is essential for the effective use of and optimal response from inhaled corticosteroid therapy. Budesonide is the preferred inhaled corticosteroid, both because more data are available on using budesonide in pregnant women than are available on other inhaled corticosteroids and because the data are reassuring. The Asthma and Pregnancy Report 1993

listed beclomethasone dipropionate as the preferred inhaled corticosteroid because, although there were few published studies on asthma medication in pregnant women, clinical experience with beclomethasone dipropionate during pregnancy was substantial--more so than with other inhaled corticosteroids. The clinical experience for beclomethasone dipropionate remains reassuring. However, published studies are now available on the use of inhaled corticosteroids, and the study data are preponderantly on budesonide. Thus, budesonide is the preferred inhaled corticosteroid for use during pregnancy because there are more data on budesonide, not because budesonide is demonstrably safer than other corticosteroid preparations. It is important to note that no data indicate that the other preparations are unsafe. Therefore, inhaled corticosteroids other than budesonide may be continued in patients who were well-controlled by these agents prior to pregnancy, especially if it is thought that changing formulations may jeopardize asthma control.

- Alternative but not preferred treatment options are presented below in alphabetical order because data are not available to allow rankings of alternative treatments relative to each other. It is important to recognize that none of these alternative treatments, either alone or together, has been demonstrated to be as effective as the therapeutic benefit of inhaled corticosteroids.
    - Cromolyn is an alternative but not preferred long-term-control medication (Level C evidence from safety studies in pregnancy) that has been used for decades as a medication for the chronic treatment of asthma and exercise-induced bronchospasm. Although the drug has limited effectiveness compared to inhaled corticosteroids, the advantage of cromolyn is its high degree of tolerance by patients and its exceptional safety profile. The safety data for use of cromolyn during pregnancy are reassuring. The Asthma and Pregnancy Report 1993 recommended initiating daily long-term-control therapy in pregnant women with cromolyn because of its excellent safety profile. Data published since 1993 on the safety and effectiveness of inhaled corticosteroids in nonpregnant patients, combined with recent reassuring safety data on the use of inhaled corticosteroids in pregnant women, warrant removing the recommendation for cromolyn and supporting the use of inhaled corticosteroid as the preferred Step 2 therapy.
    - Leukotriene receptor antagonists, including zafirlukast and montelukast, may also be considered as alternative but not preferred long-term-control medication (Level D evidence from safety studies in pregnancy). Although minimal published data exist assessing the safety of leukotriene receptor antagonists in pregnancy, and no published data assess their efficacy during pregnancy, data in animal studies submitted to the Food and Drug Administration (FDA) suggest the safety of leukotriene receptor antagonists for use during pregnancy. Similar reassurance is not available for the leukotriene synthesis inhibitor zileuton. Leukotriene receptor antagonists have been demonstrated to provide statistically significant but modest improvements when used as monotherapy in both children and nonpregnant adults. When comparing overall efficacy of leukotriene receptor antagonists to that of inhaled corticosteroids, however, most outcome measures clearly favored inhaled corticosteroids. In the opinion of the Working Group, leukotriene receptor antagonists may be

considered for use during pregnancy for patients who had a favorable response to the drug before they became pregnant. In this case, it would be preferable to maintain the therapy that successfully controlled the patient's asthma before pregnancy. However, in the opinion of the Working Group, when initiating new treatment for asthma during pregnancy, leukotriene receptor antagonists are an alternative but not preferred treatment option for mild persistent asthma.

- Sustained release theophylline preparations represent another alternative but not preferred treatment option (Levels B and C evidence from safety studies in pregnancy). Theophylline therapy has demonstrated clinical effectiveness in some studies and has been used for years in pregnant women with asthma. Theophylline is primarily a bronchodilator, and its anti-inflammatory activity demonstrated thus far is modest. However, it also has the potential for serious toxicity (nausea, vomiting, tachycardia, tachydysrhythmia, seizures) resulting from excessive dosing and/or select drug–drug interactions (e.g., with erythromycin). Thus, using theophylline during pregnancy requires careful titration of the dose and regular monitoring of serum theophylline concentrations. Timed-release preparations permit easier dosing with less fluctuation in serum theophylline concentrations. The opinion of the Working Group is that theophylline dosing should be selected to maintain serum theophylline concentrations between 5-12 micrograms/mL.

Step 3: Moderate Persistent Asthma

- The two preferred treatment options for initiating Step 3 therapy are either a combination of a low-dose inhaled corticosteroid and a long-acting inhaled $beta_2$-agonist or increasing the dose of inhaled corticosteroid to the medium-dose range. No data from studies during pregnancy clearly delineate that one option is recommended over another. On the one hand, strong evidence from clinical randomized controlled trials in nonpregnant adults favors combination therapy over increasing the dose of inhaled corticosteroid. On the other hand, only limited observational data are available on long-acting inhaled $beta_2$-agonist during pregnancy. Thus, some clinicians may prefer increasing the dose of inhaled corticosteroid, for which data on use during pregnancy exist, rather than adding a second medication.

  Preferred Step 3 treatment is either:

  - Maintain a low-dose inhaled corticosteroid and add a long-acting inhaled $beta_2$-agonist (Level C evidence from safety studies of inhaled corticosteroids in pregnancy; Level C evidence from safety studies of long-acting inhaled $beta_2$-agonists; Level D evidence from safety studies of combination therapy in pregnancy). Limited data describe the efficacy and/or safety of the use of combination therapies during pregnancy, but strong Level A evidence from effectiveness studies is found in nonpregnant adults that adding long-acting inhaled $beta_2$-agonist to a low dose of inhaled corticosteroid provides greater asthma control than only increasing the dose of corticosteroid. Although only limited

observational data are available on long-acting inhaled beta$_2$-agonists in pregnancy, there is justification for expecting long-acting inhaled beta$_2$-agonists to have a safety profile similar to that of albuterol, for which data exist on safety during pregnancy. There are no data on which to base selection of a preferred long-acting inhaled beta$_2$-agonist, but salmeterol has been available longer than others in this class of medications. When using a long-acting inhaled beta$_2$-agonist, it is important to inform the patient that this medication should not be used for the treatment of acute asthma exacerbations, should only be used in combination with an inhaled corticosteroid, and should be used at no more than the recommended dose.

Or:

- Increase inhaled corticosteroid to medium dose (Level C evidence from safety studies in pregnancy). This strategy will benefit many patients. Adverse effects, although infrequent, may arise. For example, with an increased dose, some patients may experience oral candidiasis or dysphonia, especially if they use improper inhaler technique. Inhaler technique should be reviewed regularly and whenever doses are adjusted.

  If the patient's asthma is not optimally controlled with initial Step 3 therapy, and medications are used correctly, additional therapy is recommended, particularly for patients with recurring severe exacerbations. A combination of a medium-dose inhaled corticosteroid and a long-acting inhaled beta$_2$-agonist is recommended. Referral of the patient to an asthma specialist is appropriate if there is difficulty achieving control at this step of asthma severity.

- Alternative but not preferred treatments for Step 3 care include low-dose inhaled corticosteroid and the addition of either theophylline or a leukotriene receptor antagonist (Level D evidence on safety of combination therapy in pregnancy). If necessary, increase the inhaled corticosteroid dose to within the medium-dose range. Favorable to the selection of theophylline as adjunctive therapy is the consideration that more extensive clinical experience and observational data are available and are reassuring concerning the use of theophylline during pregnancy. In the opinion of the Working Group, if theophylline is selected, serum concentrations should be maintained between 5-12 micrograms/mL.

Step 4: Severe Persistent Asthma

- Patients whose asthma is not controlled on medium dose inhaled corticosteroid along with the addition of a long-acting inhaled beta$_2$-agonist may also require oral systemic corticosteroid on a regularly scheduled, long-term basis (Level C evidence from safety studies in pregnancy).

  It is preferable to avoid the use of systemic corticosteroids if possible. Before additional medication is considered, both the patient's inhaled corticosteroid,

long-acting inhaled beta$_2$-agonist dose and the patient's technique for aerosol administration should be critically reevaluated. If additional therapy is required, the inhaled corticosteroid dose should be increased to within the high-dose range and the use of budesonide is preferred. Referral of the patient to an asthma specialist is recommended for assistance in the care of patients requiring Step 4. If the appropriate use of high-dose inhaled corticosteroid and long-acting inhaled beta$_2$-agonist is insufficient in managing symptoms, the addition of systemic corticosteroid therapy is warranted. Aggressive doses should be employed on a short-term basis (e.g., 2 mg/kg/day to a maximum daily dose of 60 mg of prednisone equivalent). For patients who require long-term systemic corticosteroid:

- Use the lowest possible dose (single dose daily or on alternate days).
- Monitor patients closely for adverse side effects of corticosteroids.
- When control of asthma is achieved, make persistent attempts to reduce the dose of or discontinue systemic corticosteroid. High-dose inhaled corticosteroid is preferable to systemic corticosteroid administration. Depending on the duration of systemic corticosteroid administration, care must be exercised in their withdrawal to avoid disease exacerbation and/or serious hypothalamic-pituitary-adrenal (HPA) crisis.
- Consultation with an asthma specialist is recommended.

Stepwise Approach for Managing Asthma During Pregnancy and Lactation: Treatment

Classify Severity: Clinical Features Before Treatment or Adequate Control		Medications Required To Maintain Long-Term Control
Symptoms/Day ---------- Symptoms/Night	PEF or FEV_1 ---------- PEF Variability	Daily Medications
Step 4 Severe Persistent		
Continual ---------- Frequent	$\leq$60% ---------- >30%	• Preferred treatment: - High-dose inhaled corticosteroid AND - Long-acting inhaled beta$_2$-agonist AND, if needed, - Corticosteroid tablets or syrup long term (2 mg/kg per day, generally not to exceed 60 mg per day) (Make repeat attempts to reduce systemic

Classify Severity: Clinical Features Before Treatment or Adequate Control		Medications Required To Maintain Long-Term Control
Symptoms/Day ---------- Symptoms/Night	PEF or FEV_1 ---------- PEF Variability	Daily Medications
		corticosteroid and maintain control with high-dose inhaled corticosteroid.*) • Alternative treatment: - High-dose inhaled corticosteroid* AND - Sustained release theophylline to serum concentration of 5–12 micrograms/mL
Step 3 Moderate Persistent		
Daily ---------- >1 night/week	>60%-<80% ---------- >30%	• Preferred treatment: EITHER - Low-dose inhaled corticosteroid* and long-acting inhaled $beta_2$-agonist OR - Medium-dose inhaled corticosteroid* If needed (particularly in patients with recurring severe exacerbations): - Medium-dose inhaled corticosteroid* and long-acting inhaled $beta_2$-agonist. • Alternative treatment: - Low-dose inhaled corticosteroid* and either theophylline or leukotriene receptor antagonist** If needed: - Medium-dose inhaled corticosteroid* and either theophylline or leukotriene

Classify Severity: Clinical Features Before Treatment or Adequate Control		Medications Required To Maintain Long-Term Control
Symptoms/Day ---------- Symptoms/Night	PEF or FEV_1 ---------- PEF Variability	Daily Medications
		receptor antagonist**
Step 2 Mild Persistent		
>2 days/week but <daily ---------- >2 nights/month	≥80% ---------- 20 to 30%	• Preferred treatment: - Low-dose inhaled corticosteroid* • Alternative treatment (listed alphabetically): cromolyn, leukotriene receptor antagonist** OR sustained-release theophylline to serum concentration of 5–12 micrograms/mL.
Step 1 Mild Intermittent		
≤2 days/week ---------- ≤2 nights/month	≥80% ---------- <20%	• No daily medication needed. • Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms. A course of systemic corticosteroid is recommended.
Quick Relief All Patients		
• Short-acting bronchodilator: 2-4 puffs short-acting inhaled $beta_2$-agonist*** as needed for symptoms • Intensity of treatment will depend on severity of exacerbation; up to 3 treatments at 20-minute intervals or a single nebulizer treatment as needed. Course of systemic corticosteroid may be needed. • Use of short-acting inhaled $beta_2$-agonist*** >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.		
Step Down Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible. Step up If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.		

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/work missed
- Maintain (near) normal pulmonary function
- Minimal use of short-acting inhaled beta$_2$- agonist***
- Minimal or no adverse effects from medications

Notes

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs (PEF is percent of personal best; FEV_1 is percent predicted).
- Gain control as quickly as possible (consider a short course of systemic corticosteroid), then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled beta$_2$-agonist*** (e.g., use of approximately one canister a month even if not using it every day indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy).
- Provide education on self-management and controlling environmental factors that make asthma worse (e.g., allergens, irritants).
- Refer to an asthma specialist if there are difficulties controlling asthma or if Step 4 care is required. Referral may be considered if Step 3 care is required.

* There are more data on using budesonide during pregnancy than on using other inhaled corticosteroids.

** There are minimal data on using leukotriene receptor antagonists in humans during pregnancy, although there are reassuring animal data submitted to FDA.

*** There are more data on using albuterol during pregnancy than on using other short-acting inhaled beta$_2$-agonists.

Pharmacologic Management of Asthma During Lactation

Prednisone, theophylline, antihistamine, inhaled corticosteroid, beta$_2$-agonist, and cromolyn are not contraindications to breastfeeding. However, maternal use of theophylline may cause irritability, feeding difficulties, or jitteriness in sensitive nursing infants. Recommendations for managing asthma during lactation are the same as those for managing asthma during pregnancy.

Pharmacologic Management of Allergic Rhinitis

Rhinitis, sinusitis, and gastroesophageal reflux disease (GERD) are conditions that are often associated with asthma, are frequently more troublesome during pregnancy, and may exacerbate coexisting asthma. If these conditions are present, appropriate treatment is an integral part of asthma management. These

topics were outside the scope of the current evidence-based review, but relevant studies on the safety of rhinitis medications during pregnancy were reviewed in order to present the following recommendations.

Based on the available data for humans as well as reassuring animal studies, loratadine or cetirizine are the current second-generation antihistamines of choice for use during pregnancy. Data on the excretion of loratadine in breast milk suggest that the amount of loratadine received by the nursing infant would not present a hazard.

Intranasal corticosteroids are the most effective medications for the management of allergic rhinitis and have a low risk of systemic effect when used at recommended doses. Although no specific safety studies of intranasal corticosteroids during pregnancy were identified, when need is indicated, their use during pregnancy is recommended, on the basis of reassuring data from studies of the oral inhaled corticosteroids. (Refer to the original guideline document for a discussion of inhaled corticosteroids.) Montelukast, a leukotriene receptor antagonist, can be used for the treatment of allergic rhinitis, but minimal data are available on the use of this drug during pregnancy.

Finally, three studies suggest that oral decongestant exposure in the first trimester may increase the risk of a rare birth defect, gastroschisis, but the absolute risk of gastroschisis in exposed fetuses is still extremely small. If nasal decongestion treatment is indicated in early pregnancy, an external nasal dilator, short-term topical oxymetazoline, or intranasal corticosteroid can be considered before use of oral decongestant.

Management of Acute Exacerbations of Asthma During Pregnancy

Home Management of Asthma Exacerbations

Asthma exacerbations have the potential to lead to severe problems for the fetus. A maternal pO_2 <60 mmHg or hemoglobin saturation <90 percent may be associated with fetal hypoxia. Therefore, asthma exacerbations in pregnancy should be managed aggressively.

Pregnant women with asthma should be taught to recognize signs and symptoms of early asthma exacerbations, such as coughing, chest tightness, dyspnea, wheezing, or a 20 percent decrease in their PEF rate. A decrease in fetal movement may be an early manifestation of an asthma exacerbation. Early recognition of worsening asthma is important so that prompt home rescue treatment may be instituted to avoid maternal and fetal hypoxia. Patients should be given an individualized guide for decision making and rescue management. In general, home treatment begins with inhaled albuterol (2-4 puffs every 20 minutes for up to 1 hour). A good response is characterized by symptoms that are resolved or become subjectively mild, the ability to resume normal activities, and PEF rate >80 percent of personal best. The patient should seek further medical attention promptly if the response is incomplete or if fetal activity is decreased. (See Appendix B, figure 4 in the original guideline document.)

Hospital and Clinic Management

Recommendations for assessment and treatment of exacerbations in the hospital and clinic setting are presented in appendix B, figure 5 of the original guideline document, and usual drug dosages for asthma exacerbations are presented in figure 6. The prevention of maternal and fetal hypoxia is the principal goal. Continuous electronic fetal monitoring should be considered when the fetus is potentially viable. Albuterol delivered by nebulizer (2.5 mg = 0.5 mL albuterol in 2.5 mL normal saline driven with oxygen) is recommended; treatments should be given every 20 minutes in the first hour. Oral systemic corticosteroids should be given to patients with FEV_1 or PEF above 50 percent predicted if there is no immediate response to albuterol or if the patient recently took oral corticosteroids; corticosteroids should be given orally for patients with lower FEV_1 or PEF and intravenously for those with impending respiratory arrest. In addition to albuterol, oxygen to achieve oxygen saturation $\geq$95 percent is recommended for all patients.

Ipratropium bromide, an anticholinergic, is recommended as additional therapy in severe exacerbations. No published data on anticholinergics in pregnancy were available for the current evidence review. However, studies show minimal absorption of quaternary amines from the lung. Considering the inhalation route of administration and reassuring experimental animal studies submitted to the FDA, ipratropium bromide can be recommended for use during pregnancy.

In the opinion of the Working Group, the patient should be assessed for pulse rate, use of accessory muscles, wheezing, and FEV_1 and/or PEF rate before and after each bronchodilator treatment. Measurement of oxygenation via pulse oximeter or arterial blood gases is essential. Arterial blood gas measurements should be obtained if the patient is in severe distress. Chest x rays should not be routinely obtained. Repeat assessment of patients with severe exacerbations is recommended after the initial dose of inhaled $beta_2$-agonist, and repeat assessments of all patients are recommended after three doses (60-90 minutes after initiating the treatment). Inhaled corticosteroid should be continued if the patient was already taking inhaled corticosteroid, or an inhaled corticosteroid should be initiated at discharge from the emergency department or hospital (e.g., as part of discharge planning during hospitalization). The rationale for introducing an inhaled corticosteroid is that this treatment reduces recurrent exacerbations in pregnant women with asthma.

Management of Asthma During Labor and Delivery

Asthma medications should be continued during labor and delivery. Although asthma is usually quiescent during labor, consideration should be given to assessing PEF rates on admission and at intervals during labor. If systemic corticosteroid has been used in the previous 4 weeks, then stress-dose steroid (e.g., hydrocortisone 100 mg every 8 hours, intravenously) should be administered during labor and for the 24-hour period after delivery to prevent maternal adrenal crisis.

Rarely, if ever, is it necessary to deliver a fetus via cesarean due to an acute exacerbation of asthma. Usually, maternal and fetal hypoxia can be managed by optimal medical management. Occasionally, delivery may improve the respiratory status of a patient who has unstable asthma and is near term. Prostaglandin (PG) E_2 or E_1 can be used for cervical ripening, the management of spontaneous or

induced abortions, or postpartum hemorrhage. However, 15-methyl PGF_2- alpha and methylergonovine can cause bronchospasm. Magnesium sulfate, which is a bronchodilator, and beta-adrenergic agents such as terbutaline can be used to treat preterm labor. Indomethacin, however, can induce bronchospasm in the aspirin-sensitive patient. No reports were found of the use of calcium channel blockers for tocolysis among patients with asthma.

Epidural analgesia has the benefit of reducing oxygen consumption and minute ventilation during labor. Meperidine causes histamine release but rarely causes bronchospasm during labor. A 2 percent incidence of bronchospasm has been reported with regional anesthesia. Communication between the obstetric, anesthetic, and pediatric caregivers is recommended.

Definitions:

Evidence Category A: Randomized controlled trials, rich body of data. Evidence is from the endpoint of well-designed randomized controlled trials that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.

Evidence Category B: Randomized controlled trials, limited body of data. Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of randomized controlled trials, or meta-analysis of randomized controlled trials. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendations, or the results are somewhat inconsistent.

Evidence Category C: Nonrandomized trials and observational studies. Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.

Evidence Category D: Panel consensus judgment. This category is used only where the provision of some guidance was deemed valuable, but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The consensus is based on clinical experience or knowledge that does not meet the criteria for categories A through C.

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Management of Asthma Exacerbations during Pregnancy and Lactation: Home Treatment
- Management of Asthma Exacerbations during Pregnancy and Lactation: Emergency Department and Hospital-Based Care

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on the Working Group's interpretation of the current scientific review of the evidence on the safety of asthma medications during pregnancy and consideration of previous National Asthma Education and Prevention Program (NAEPP) reports: the Asthma and Pregnancy Report 1993, the Expert Review Panel (EPR)-2 1997, and the EPR-Update 2002.

The type of supporting evidence is identified and graded for some of the recommendations (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Provision of optimal therapy to maintain control of asthma for maternal health and quality of life as well as for normal fetal maturation

POTENTIAL HARMS

- Theophylline has the potential for serious toxicity (nausea, vomiting, tachycardia, tachydysrhythmia, seizures) resulting from excessive dosing and/or select drug-drug interactions (e.g., with erythromycin).
- Maternal use of theophylline may cause irritability, feeding difficulties, or jitteriness in sensitive nursing infants.
- Depending on the duration of systemic corticosteroid administration, care must be exercised in their withdrawal to avoid disease exacerbation and/or serious hypothalamic-pituitary-adrenal (HPA) crisis.
- Oral corticosteroid use during pregnancy in patients who have asthma is associated with an increased incidence of preeclampsia and the delivery of both preterm and low birth weight infants. The available data, however, make it difficult to separate the effects of the corticosteroids on these outcomes from the effects of severe or uncontrolled asthma. Moreover, because severe asthma has been associated with maternal and/or fetal mortality, risk-benefit considerations favor the use of oral corticosteroid medication when indicated in the long-term management of severe asthma or severe exacerbations during pregnancy.
- See section IIA in the original guideline document for a full discussion of "Considerations in Evaluating Medication Effects on Pregnancy Outcome."

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The recommendations made in Asthma and Pregnancy -- Update 2004 are intended to assist clinical decision making; the clinician and patient still need to develop individual treatment plans that are tailored to the specific needs and circumstances of the pregnant woman. The National Asthma Education and Prevention Program (NAEPP), and all who participated in the development of this latest report, hope that the pregnant woman with asthma and her newborn will be the beneficiaries of the recommendations in this document. This report is not an official regulatory document of any government agency.

- Although it is preferable to use data on humans to estimate human risk, studies in humans may not be practical or informative. The most highly valued study design for evaluating drug therapy, the randomized controlled trial, is often avoided in pregnant subjects, particularly for medications for which the effects on pregnancy are not well characterized. Often, human data are restricted to pregnancy outcome after inadvertent exposure to a medication during an unplanned pregnancy. These human reports may be limited in their interpretability. (See section IIA in the original guideline for a full discussion of "Considerations in Evaluating Medication Effects on Pregnancy Outcome.")
- Recommendations for pharmacologic therapy are intended to be general guidelines to assist clinical decision making. They are not intended to be prescriptions for treatment or to replace individualized treatment plans. Asthma is highly variable. Specific therapy should be tailored to the needs and circumstances of individual patients.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Asthma Education and Prevention Program. Managing asthma during pregnancy: recommendations for pharmacologic treatment. Bethesda (MD): National Heart, Lung, and Blood Institute; 2005 Jan. 57 p. [129 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency [U.S.]

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National Heart, Lung, and Blood Institute (NHLBI)

GUIDELINE COMMITTEE

Working Group on Managing Asthma During Pregnancy

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Working Group Members: William W. Busse, MD (Chair), University of Wisconsin Medical School, Madison, WI; Michelle Cloutier, MD, Connecticut Children's Medical Center, Hartford, CT; Mitchell Dombrowski, MD, St. John Hospital, Detroit, MI; Harold S. Nelson, MD, National Jewish Medical and Research Center, Denver, CO; Michael Reed, PharmD, Rainbow Babies and Children's Hospital, Cleveland, OH; Michael Schatz, MD, MS, Kaiser-Permanente Medical Center, San Diego, CA; Anthony R. Scialli, MD, Georgetown University Hospital, Washington, DC; Stuart Stoloff, MD, University of Nevada School of Medicine, Reno, NV; Stanley Szefler, MD, National Jewish Medical and Research Center, Denver, CO

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Busse has served on the Speakers' Bureaus of Aventis, GlaxoSmithKline, and Merck; he has served on the Advisory Boards of AstraZeneca, Aventis, Pfizer, and Schering; he has received funding/grant support for research projects from Aventis, Fujisawa, GlaxoSmithKline, Hoffmann LaRoche, Pfizer, and Wyeth; he has served as a consultant for Bristol-Myers Squibb, Dynavax, Fujisawa, Hoffmann LaRoche, and Wyeth.

Dr. Cloutier has received funding/grant support for research projects from GlaxoSmithKline.

Dr. Dombrowski has none.

Dr. Nelson has served on the Speakers' Bureaus of AstraZeneca and GlaxoSmithKline; he has received funding/grant support for research projects from Altana, AstraZeneca, Dey Laboratories, Eli Lilly, Epigenesis, and IVAX; he

has served as a consultant for Altana, AstraZeneca, Aventis, Dey Laboratories, Dynavax Technologies, Genentech, GlaxoSmithKline, Integrated Therapeutics Group, Protein Design Laboratories, Rigel Pharmaceuticals, UCB, and Wyeth.

Dr. Reed has served on the Speakers' Bureaus of Abbott Laboratories, Bristol-Myers Squibb, Enzon, GlaxoSmithKline, Pfizer, Roche, and Somerset; he has received funding/grant support for research projects from Health Resources and Services Administration, National Institutes of Health, Abbott Laboratories, AstraZeneca, Aventis, Bristol-Myers Squibb, Eli Lilly, Forrest Laboratories, GlaxoSmithKline, Janssen, Johnson & Johnson, Merck, Novartis, Organon, Pfizer, Roche, Schering, Somerset, and Wyeth-Ayerst; he has served as a consultant for Abbott Laboratories, Bristol-Myers Squibb, Enzon, GlaxoSmithKline, Pfizer, and Somerset.

Dr. Schatz has served on the Speakers' Bureaus of AstraZeneca and Merck; he has received funding/grant support for research projects from Aventis and GlaxoSmithKline.

Dr. Scialli has none.

Dr. Stoloff has served on the Speakers' Bureaus of Alcon, AstraZeneca, Aventis, Genentech, GlaxoSmithKline, Pfizer, and Schering; he has served as a consultant for Alcon, AstraZeneca, Aventis, Genentech, GlaxoSmithKline, Pfizer, and Schering.

Dr. Szefler has received funding/grant support for research projects from the National Institutes of Health, AstraZeneca, and Russ Pharmaceuticals; he has served as a consultant for AstraZeneca, Aventis, GlaxoSmithKline, and Merck.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the National Heart, Lung, and Blood Institute (NHLBI) Web site.

Print copies: Available from the NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: nhlbiic@dgsys.com.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Quick reference from the Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment. 12p. 2004. Available in Portable Document Format (PDF) from the National Heart, Lung, and Blood Institute (NHLBI) Web site.
- Managing asthma during pregnancy: recommendations for pharmacologic treatment -- Update 2004. Evidence tables. 59 p. 2004. Available in Portable

Document Format (PDF) from the National Heart, Lung, and Blood Institute (NHLBI) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on February 15, 2005. This summary was updated by ECRI on December 5, 2005 following the U.S. Food and Drug Administration (FDA) advisory on long-acting beta2-adrenergic agonists (LABA).

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